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(71) Applicant (for all designated States except US): UAB RESEARCH FOUNDATION [US/US]; 701 South 20th, Street, Suite 1120G, Birmingham, AL 35294 (US).

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(72) Inventors; and

(75) Inventors/Applicants (for US only): SCHWIEBERT, Erik [US/US]; 2805 Glenstone Lane, Birmingham, AL 35242 (US). ZSEMBERY, Akos [HU/US]; 1917F Tree Top Lane, Birmingham, AL 35216 (US).

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(74) Agents: McKEON, Tina, Williams et al.; Needle & Rosenberg, P.C., Suite 1000, 999 Peachtree Street, Atlanta, GA 30309-3915 (US).

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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM,

(54) Title: METHODS AND COMPOSITIONS FOR P2X RECEPTOR CALCIUM ENTRY CHANNELS AND OTHER CALCIUM ENTRY MECHANISMS

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(57) Abstract: This invention relates generally to a method of increasing cytosolic Ca<sup>2+</sup> levels in mammalian cells comprising contacting P2X receptor Ca<sup>2+</sup> entry channels or any and all other Ca<sup>2+</sup> entry channels or mechanisms on the cell with an effective amount of a small molecule, and a composition comprising the small molecule in a delivery system. The invention has broad applicability in the pharmaceutical industry as a method of treating airway diseases (such as cystic fibrosis and asthma), ailments of the lung and airways (such as those caused by common cold pathogens or allergens in allergy), kidney diseases and renal hypertensive disorders (such as polycystic kidney disease and salt-sensitive hypertension syndromes), and endocrine disorders (such as diabetes).

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/01298

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 31/315, 33/00, 49/00; A61P 3/08, 3/10, 3/14, 7/00, 11/00, 11/02, 31/00; G01N 33/50, 33/53  
 US CL : 424/9.2, 641, 643; 514/494, 849, 851, 866; 435/7.21

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
 U.S. : 424/9.2, 641, 643; 514/494, 849, 851, 866; 435/7.21

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
 Please See Continuation Sheet

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5,840,278 A (COLEMAN) 24 November 1998 (24.11.1998), column 1, line 42 to column 2, line 7, see claims 1-5.	1-2,5,10,12-13,16,18,21-22,24-25,29,31,34-35
Y	TAYLOR, A.L. et al. Epithelial P2X purinergic receptor channel expression and function. Journal of Clinical Investigation. October 1999, Vol. 104, No. 7, pages 875-884.	1-41
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A		
Y	SCHWIEBERT, E.M. et al. Extracellular nucleotide signaling along the renal epithelium. American Journal of Physiology. June 2001, Vol. 280, No. 6, Part 2, pages F945-F963.	1-41, 48-135
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A		
Y	Database CAPLUS on STN, American Chemical Society, (Columbus, Ohio, USA), No. 2001:30580, SPERLAGH, B. et al. 'Local regulation of [3H]-noradrenaline release from the isolated guinea-pig right atrium by P2X-receptors located on axon terminals,' abstract, British Journal of Pharmacology, 2000.	1-41
Y	US 5,834,032 A (SONG) 10 November 1998 (10.11.1998), see claim 1.	45-47 and 138-141

<input checked="" type="checkbox"/>	Further documents are listed in the continuation of Box C.	<input type="checkbox"/>	See patent family annex.
* Special categories of cited documents:			
"A"	document defining the general state of the art which is not considered to be of particular relevance	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
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"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O"	document referring to an oral disclosure, use, exhibition or other means	"&"	document member of the same patent family
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Mail Stop PCT, Attn: ISA/US  
 Commissioner for Patents  
 P.O. Box 1450  
 Alexandria, Virginia 22313-1450  
 Facsimile No. (703) 305-3230

Authorized officer

JOHN PAK

*Janulal Shabir Jr*

Telephone No. (703)308-1235

**INTERNATIONAL SEARCH REPORT**

International application No.  
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**C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y -- A	SCHWIEBERT, E.M. et al. Autocrine extracellular purinergic signaling in epithelial cells derived from polycystic kidneys. American Journal of Physiology. April 2002, Vol. 282, No. 4, Part 2, pages F763-F775.	48-135 ----- 44, 136-137
A	Database CAPLUS on STN, American Chemical Society, (columbus, Ohio, USA), No. 2000:11454, SOHNLE, P.G. et al. 'Effect of zinc-reversible growth-inhibitory activity in human empyema fluid on antibiotic microbicidal activity,' abstract, Antimicrobial Agents and Chemotherapy, 2000.	42-43

**INTERNATIONAL SEARCH REPORT**

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Continuation of B. FIELDS SEARCHED Item 3:  
STN ONLINE, File Caplus Medline. Search Terms: zinc, diabetes, cystic fibrosis, P2X, calcium, epithelial, polycystic, pkd.